The Use of Botulinum Toxin in Abdominal Wall Reconstruction: A Case Series

An Honors Thesis (HONR 499)

by

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Abstract

Introduction: Fascial closure may pose challenges in AWR but is associated with decreased rates of hernia recurrence, surgical site infection and mesh infection. Preoperative Botulinum toxin A (BTA) injection causes temporary muscle paralysis and may be used as an adjunct in AWR. There are few published reports on this subject. We describe four unique, complex cases in which BTA can successfully be used to facilitate abdominal wall closure.
Methods: Four unique cases from the Carolinas Medical Center (CMC) in which preoperative image-guided BTA injections were administered to the lateral abdominal wall musculature were reviewed. Demographics, hernia characteristics, imaging, surgical technique, complications and outcomes were evaluated.
Results: For the four cases, the average BMI was 29.15±3.9kg/m2, age 58±14.8years, and they had 1.3±0.4 previous hernia repairs. Three patients had large ventral hernias, and one had a flank hernia. One patient had a previous external oblique component separation. Average operative data included: time to surgery from BTA injection: 29.3±2.7 days, operative time: 252.8±101.4min, defect size: 397±279.3cm2, mesh size: 1104.8±365.2cm2. Mid weight polypropylene mesh was used in all cases and primary fascial closure was achieved in all patients. There were no postoperative complications. With an average follow up time of 18±12.8 months, there are no recurrences.
Conclusion: BTA injection into the lateral abdominal wall musculature should be considered in certain challenging AWR cases in order to reapproximate the muscular fascia. Preoperative BTA injection appears to be a minimally invasive, safe, and effective technique in facilitating primary fascial closure in cases where component separation may not be adequate, possible, or previously failed.

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Process Analysis Statement

During the summer of 2016, I was fortunate enough to be selected for an internship with the Carolinas Laparoscopic and Advanced Surgery Program at the Carolinas Medical Center in Charlotte, North Carolina. Through this opportunity, I was able to observe lab testing for active and ongoing studies, shadow surgeons in the operating room, contribute to weekly research meetings, and work closely with world-class physicians on research projects. The main research project I became involved with had to do with examining the novel use of Botulinum Toxin A (Botox) in complex abdominal wall reconstruction cases – this is where the idea for this thesis came from. I was given the arduous task of combing through medical records of all recent patients who had undergone this procedure, and then conducting a retrospective chart review and analysis of each one.

Over the span of ten weeks, not only did I have to collect and analyze large amounts of data for each patient, but I also had to do a vast amount of research on the background of the procedure itself. As a college student with very minimal medical experience compared to the physicians I was working with, I came into this project at a severe disadvantage from a knowledge perspective, and had to face the challenge of simply not knowing much of what my mentors considered basic information. To combat this challenge, I dedicated a majority of my time to research – I researched the Botulinum Toxin itself, the theory and process of an abdominal wall reconstruction, surgical terminology, how Botox was administered, how to efficiently read a medical chart, etc. Through many hours of sifting through articles, observing the procedures being performed, asking questions, and analyzing data, I became incredibly well versed in a very unique procedure that has only been performed a handful of times throughout the entire world. After my internship ended, I simply wasn't ready to forego my involvement. When I returned to Ball State for my senior year, I told the physicians in Charlotte that I wanted to keep working on the project I had invested so much time in and began finishing up the research and writing a manuscript. Thus, my thesis was born.

Throughout this long process, I have grown immensely as a researcher and a writer. Clinical research has always been an interest of mine, and I hope to make it an integral part of my future medical career. Receiving the opportunity to work with and be mentored by such distinguished medical professionals as these has not only opened my eyes to the importance of clinical research, but has also taught me the best ways to conduct it – an invaluable asset as I enter into medical school. This thesis is essentially the culmination of everything I have learned thus far involving research and scientific writing, and I consider it to be the official beginning of my medical career.

Introduction

Incisional ventral hernias occur in approximately 20% of all patients undergoing laparotomy[1,2,3], a rate that has been show to increase by as much as 15% in higher risk patients who suffer from obesity and other comorbidities[4,5]. Despite advances in surgical technique and the utilization of mesh, the rate of hernia recurrence continues to be significant, especially for patients who have undergone previous failed repair and have larger defects as the size of defect is largely correlated with the risk of recurrence and chance of hernia repair failure[6]. Cost associated with repair of ventral hernias and complications arising from them are substantial[7]. Poulose et al.[7] examined the number of ventral hernia repairs performed in the US and their associated costs from 2001-2006, and found that even a 1% reduction in recurrence rates and the need for reoperation would save $32 million annually. The second most common reason for readmission to the hospital after any surgical procedure in the United States is a VHR[8]. In an assessment of 794 patients, Holihan et al.[9] demonstrated that patients who had undergone multiple previously failed repairs had a higher rate of reoperation, surgical site infection, operative duration, and hernia recurrence – the authors demonstrated a 73% recurrence rate in patients who underwent their third incisional hernia repair[9].

Abdominal wall reconstruction for complex ventral hernias can often be challenging due to loss of domain, size of hernia, and previous abdominal wall reconstruction. Loss of domain of the abdominal wall refers to cases in which at least 15-20% of the intraabdominal contents are outside the peritoneal cavity[10,11]. It is an issue often encountered in complex hernia repair procedures[11], and one that remains a significant challenge to abdominal wall closure due to having to replace the contents of the hernia sac to the abdominal cavity, leading to increased abdominal wall tension[12]. In addition to difficulties when performing fascial closure, abdominal wall tension leads to increased postoperative morbidity and hernia recurrence[6,13]. Excessive abdominal wall tension after VHR may result in a recurrence through disruption of the midline and subsequent lateral abdominal wall muscular contraction, followed by retraction of the fascial edges[14]. Bridging or inlay mesh repair of ventral hernia defects carries a high recurrence rate and has demonstrated to be inferior to sublay, retrorectus and onlay mesh placement positions with regard to recurrence and surgical site infections [15-18]. Efforts to achieve fascial closure over mesh repair include component separation. While myofascial component separation successfully accomplishes release of the scarred and restricted abdominal wall[14], some patients will require additional advancement to allow myofascial reapproximation. Furthermore, no standard of care or long term evaluations exist to indicate the safety of rereleasing the oblique musculature.

McAdory et al.[19] and others have attempted to combat this issue using progressive preoperative pneumoperitoneum (PPP) as a pneumatic tissue expander, pressurizing the abdomen to prepare patients with loss of domain for repair. While the overall recurrence rate associated with PPP use has been shown to range from 2.6-5%[,19,20,21], it does have increased costs and risks like pulmonary mycetoma, deep venous thrombosis, acute renal failure, port infection, and others[19]. In addition, Sabbagh et al[13] demonstrated that PPP can also stretch the muscles and hernia sac, especially in cases where the abdominal muscles are significantly retracted.

Intraabdominal injections of Botulinum Toxin A (BTA) have been shown to improve outcomes and reduce muscle tension. BTA is a neurotoxin isolated from the bacterium *Clostridium botulinum*[14]. It is most commonly used for cosmetic procedures, dystonias, some pain management, and spasticity related disorders[7]. BTA functions by acting as a cholinergic neuromuscular antagonist, which obstructs the release of acetylcholine at the neuromuscular junction, leading to short term flaccid muscle paralysis for up to 6 months[22,23]. In a prospective study of 27 patients undergoing ultrasound guided BTA injections, Elstner et al.[6] described that BTA can be used as an aide for myofascial relaxation in the lateral wall of the abdomen, lengthening and thinning the muscles. Abdominal oblique muscle paralysis has been shown to decrease fascial defects and facilitate abdominal wall closure with minimal tension[6].

While several studies have described the effect BTA has on fascial closure, lateral abdominal muscle length and thickness, and post-operative pain, there is very minimal literature that reviews BTA's effect on hernia recurrence, especially in higher risk patients. We report a series of four unique cases of abdominal wall reconstruction where BTA injection to the lateral abdominal musculature was used to minimize the rate of hernia recurrence and postoperative complications, as there were no other reconstructive options available to obtain myofascial reapproximation.

Methods

Four unique cases where BTA was utilized were selected to demonstrate the utility of Botox in cases where other reconstruction methods were not favorable. Approximately one month prior to surgery, the patients presented to interventional radiology and underwent CT guided BTA injections into the lateral abdominal wall musculature. Local anesthetic was utilized and 22-gauge spinal needles were advanced into anterior and posterior sections of the transverse abdominis, internal oblique, and external oblique muscles. The amount of BTA varied for each case, ranging from 100- 300 units (5 units/cc sterile saline) and 2-4 equidistant sites were selected near the rib cage and iliac crest on each side of the abdomen depending on the specific case. On average, 150 units were injected per side, with about 7 units per injection.

Measurements of the hernia sac volume (HSV) and abdominal cavity volume (ACV) as well as the volume ratio (VR=HSV/ACV) were obtained as described by Tanaka et al.[24] for the patients with a loss of domain (Patient 1 and 4).

Case Reports

Case 1

A 61-year-old man with extensive history of trauma and a previously failed hernia repair with associated postoperative infection presented to our hernia referral center with a massive ventral hernia with loss of domain including patients entire small and large intestine, stomach, and part of pancreas (Fig. 1 & 2). The patient's BMI was 33 kg/m^2, and he had a history of coronary artery disease and tobacco use. On CT (Fig. 2)

maximal width of the defect was 17 cm. The hernia volume ratio was 16.5%. [Hernia (cc x ap x transverse) =20.6 x 6.9 x 17.6; Abdomen =38.9 x 12.6 x 30.9; HSV=1300.9; ACV=7875.6; VR=16.5%].

Given the extensive size of the defect and large loss of domain, the patient was counseled to lose weight preoperatively and BTA injections were recommended to facilitate abdominal closure.

The patient lost 22 pounds, quit smoking, and presented for surgery one month after the BTA injections. He underwent an open ventral hernia repair with mesh, including bilateral external oblique and posterior rectus sheath release. Intraoperatively, the defect measured 29x27cm, and mesh overlap was achieved by sewing two 25x35cm meshes together to make a 50x35cm mesh. The mesh was placed in a preperitoneal location and fascia was closed over the mesh in the midline. The patient has had no wound complications and no recurrence within 3 months of follow up.

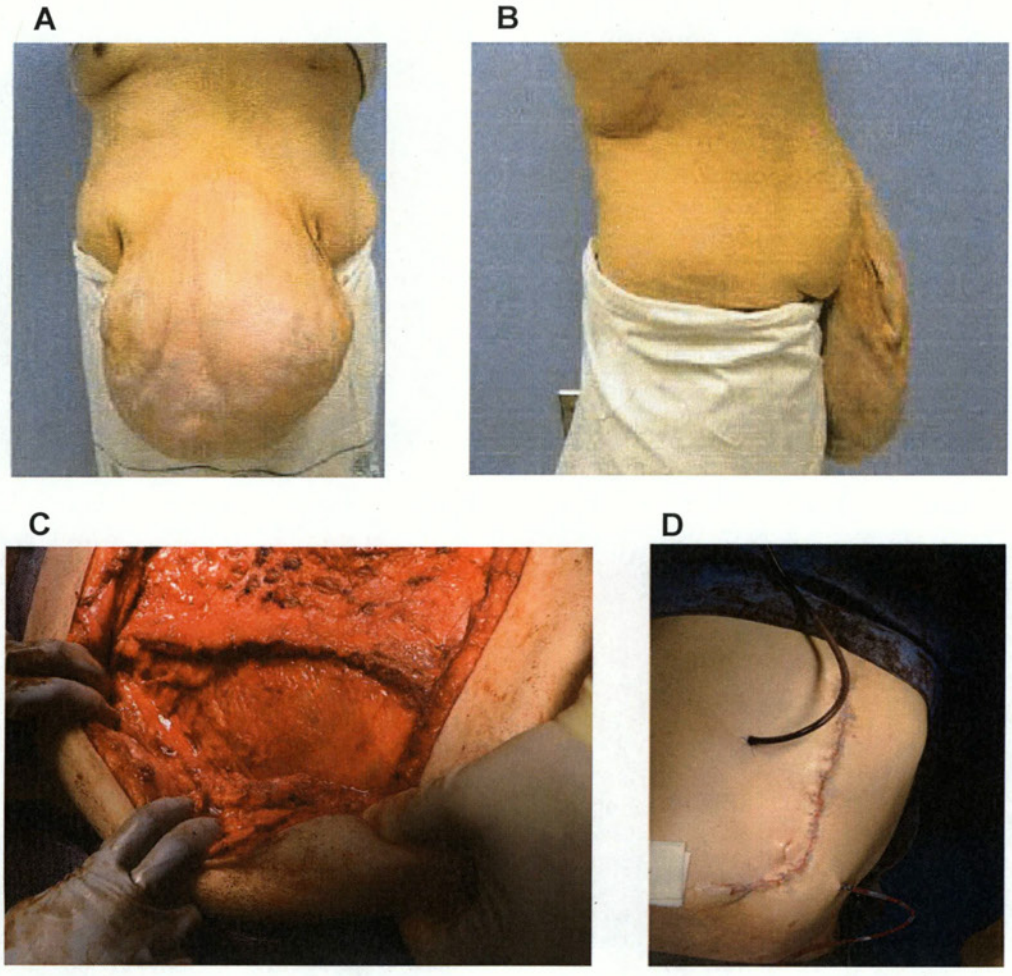

Figure 1.
Case 1: Preoperative ventral photograph **A**, Preoperative lateral photograph **B**, Intraoperative photographs **C** & **D**

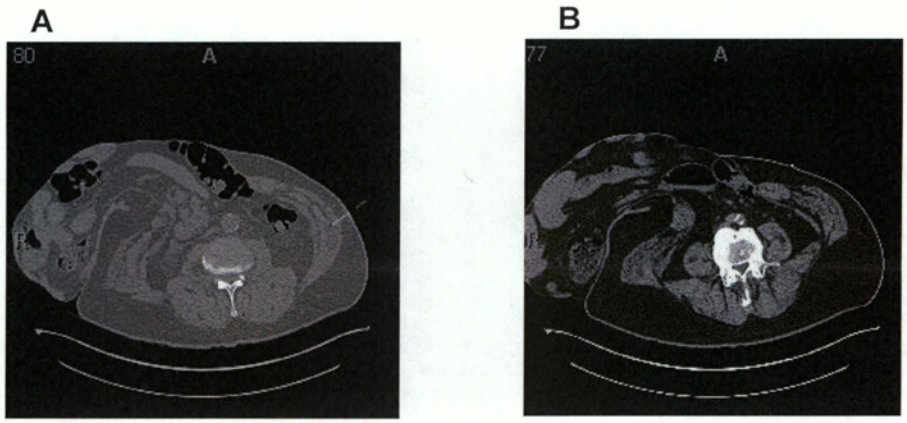

Figure 2.
Case 1: Preoperative CT scans **A** & **B**

Case 2

A 75-year-old woman with history of right colectomy and two subsequent failed ventral hernia repairs, including a bilateral external oblique myofascial release. She presented with a multiply recurrent right abdominal wall hernia (Fig. 4). Her BMI was 22.89 kg/ m2 and the defect measured 13 x 10 cm on CT (Fig. 3). Due to the large defect to body size ratio and a previously failed component separation, BTA injections were recommended.

The patient presented for surgery one month after the BTA procedure. She underwent an open ventral hernia repair with preperitoneal mesh. The mesh was 30x29 cm and the fascia was closed without the need to perform myofascial release. The patient did not have any postoperative wound complications and there has been no evidence of hernia recurrence with one year of follow up.

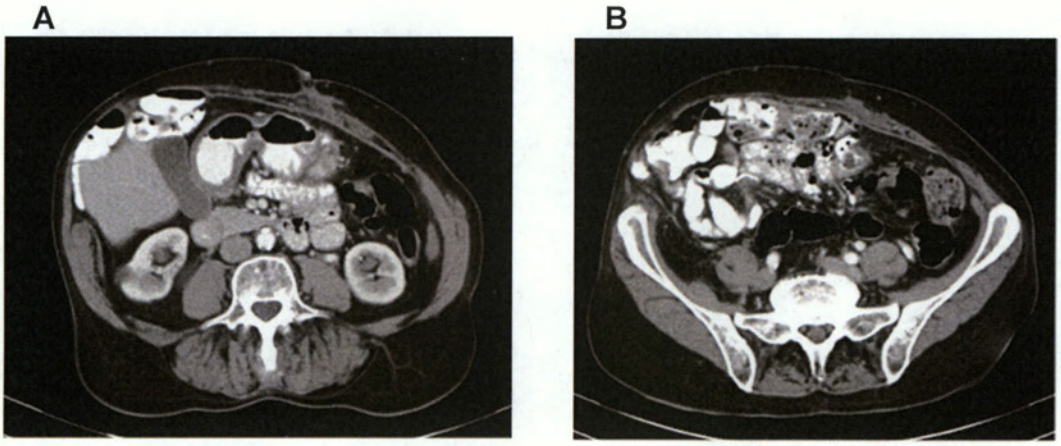

Figure 3.
Case 2: Preoperative CT images **A** & **B**

Figure 4.
Case 2: Preoperative photograph of right abdominal wall hernia

Case 3

A 57-year-old man with history of open right partial nephrectomy for renal cell cancer in 2011 and subsequent flank hernia presented with a symptomatic, recurrent flank hernia. The patient had a previous failed repair in 2012 with polypropylene mesh. He had a large lateral defect measuring 10 cm on CT (Fig. 5A) as well as retraction of his oblique muscles to his iliac crest. The width of his right oblique muscles was almost five centimeters due to the muscle retraction. His BMI was 29.02 kg/m2. Because of the extensive contraction of the lateral abdominal wall musculature, BTA injections were recommended and only required on one side of the abdomen.

The patient presented for surgery one month after the procedure, having lost 9 lbs, and underwent an open flank hernia repair. The defect measured 13x10cm and a 28x28cm mesh was used in the preperitoneal position. No component separation was needed to accomplish closure of this lateral defect. He had no postoperative complications and at 23-month follow-up, there has been no evidence of recurrence.

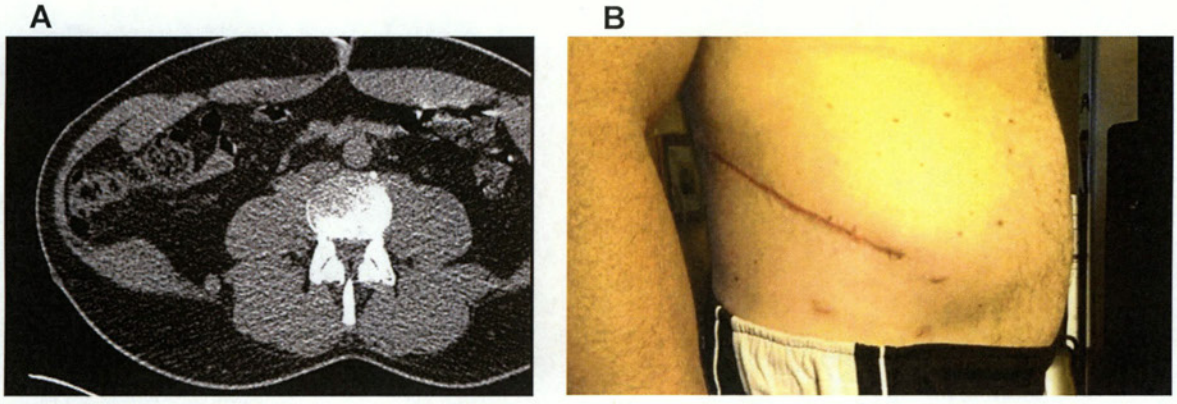

Figure 5.
Case 3: Preoperative CT **A,** Postoperative photograph **B**

Case 4

A 32-year old man with history of blunt abdominal trauma from a fall, multiple laparotomies, and eventual takedown of enterocutaneous fistula, presented with a large abdominal wall defect and loss of domain (Fig 6A & 6B). The patient's BMI was 31.17 kg/m2 and on CT (Fig. 6C) the defect width measured 15.5 cm. The hernia volume ratio was 22.4%. [Hernia (cc x ap x transverse) =30.5 x 5.5 x 15.5; Abdomen =40.2 x 11.9 x 24.3; HSV=1352.1; ACV=6044.8; VR=22.4%]

BTA injections were recommended. One month post BTA, a repeat CT was obtained demonstrating a defect size decrease by 30% (from 15.5 cm to 10 cm in width). The patient subsequently had an open ventral hernia repair with mesh. Intraoperatively, the defect measured 15x25cm and a bilateral transversus abdominus muscle release was performed to facilitate midline closure over a 30x35cm mid weight polypropylene mesh. The patient did not have any postoperative wound complications or recurrence at 6 months follow up.

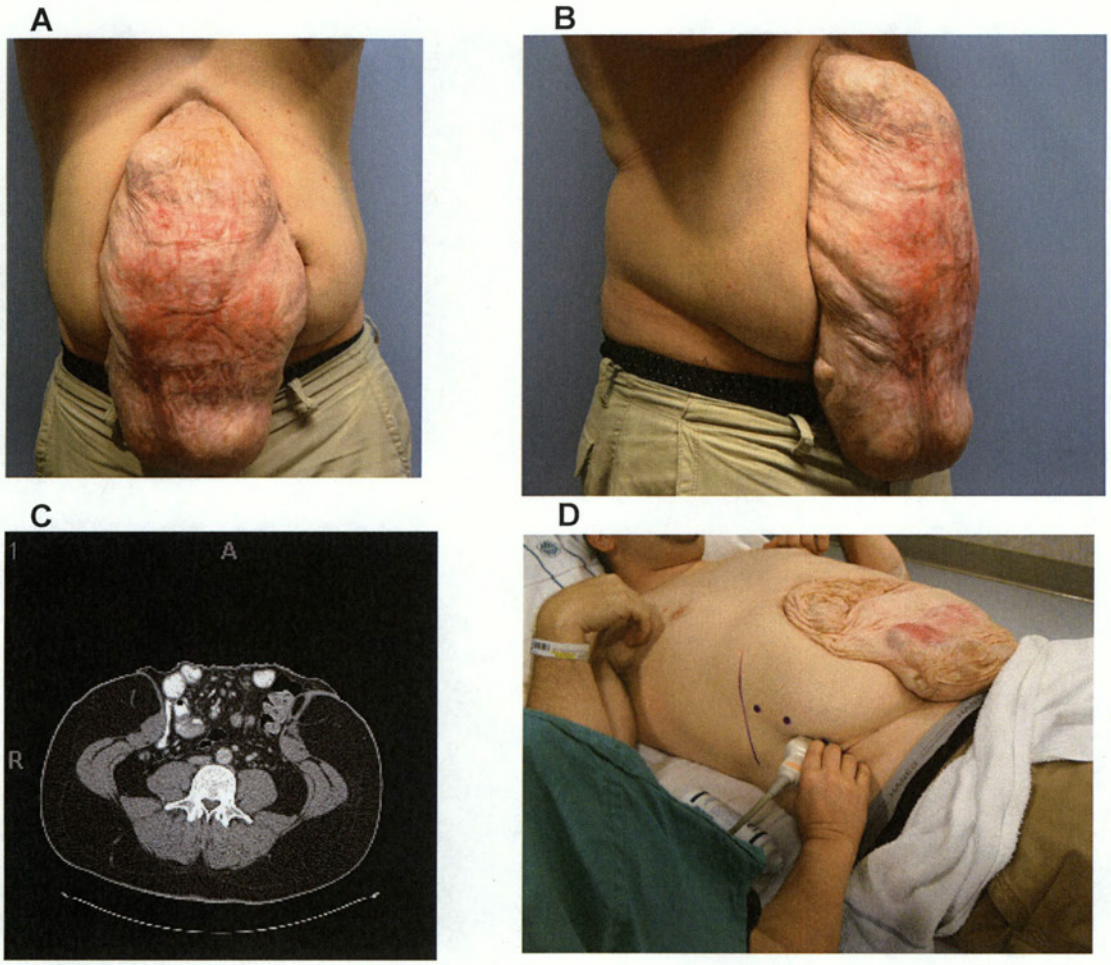

Figure 6.
Case 4: Preoperative ventral photograph**A,** Preoperative lateral photograph B, Preoperative CT **C**, BTA injection before ventral hernia repair **D**

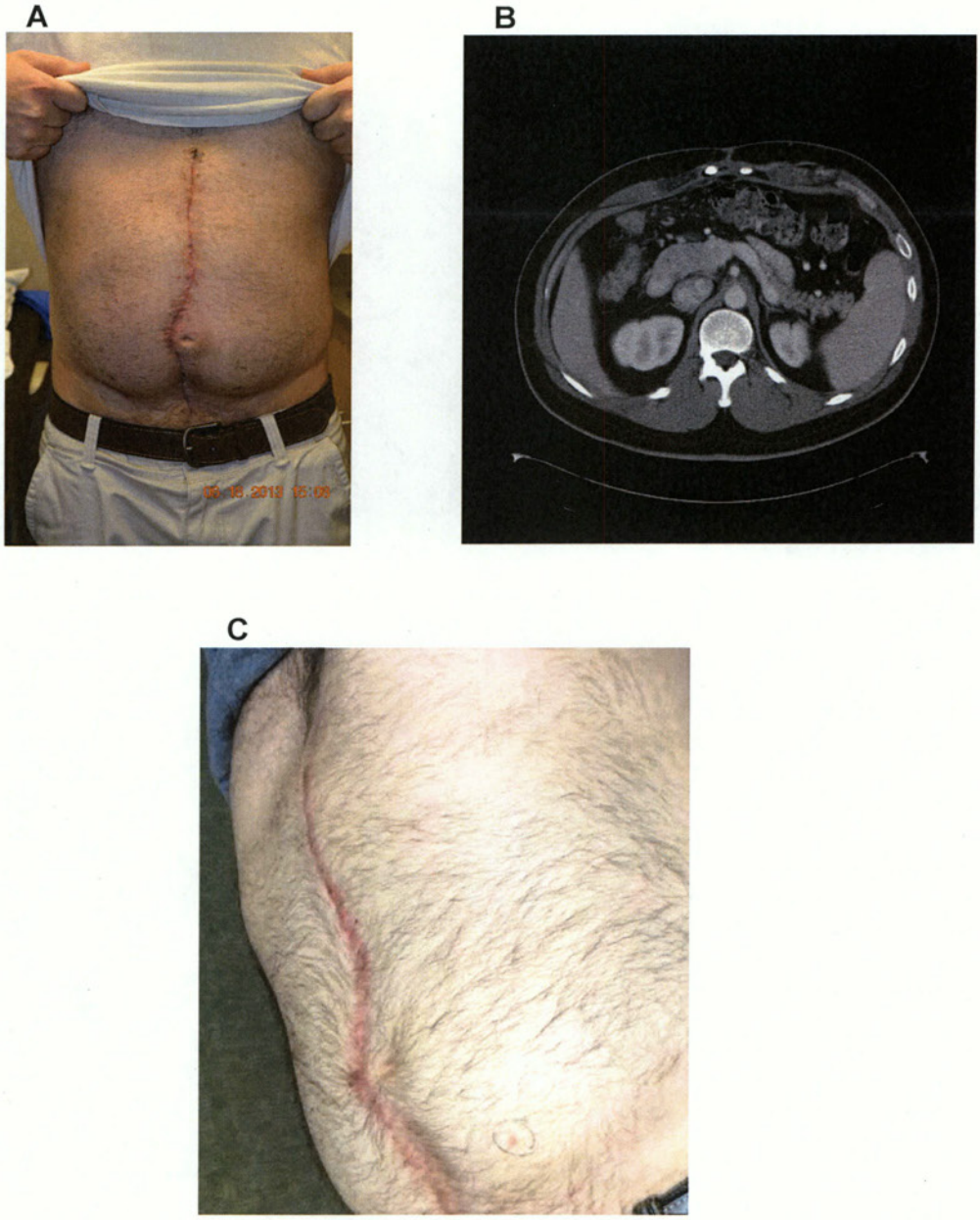

Figure 7.
Case 4: 4 weeks postoperative **A,** 6 month postoperative CT **B**, 1 year postoperative photograph **C**

Results

Four unique hernias are presented here to demonstrate the utilization of pre-operative BTA injections to the abdominal wall musculature and subsequent abdominal wall reconstruction. Mean age was 58±14.8 years (range 35-62). Mean BMI at initial consultation was 29.15±3.9 kg/m^2 (range 22-33) and 26.45±2.5 kg/m^2 at the time of operation after preoperative weight loss. All 4 patients had at least one previous failed repair (mean 1.3±0.4) with one patient having had previous external oblique component separation. The mean defect area was 397±279.3 cm^2 (range 130-783 cm^2) and the average mesh size 1104.8±365.2 cm^2. BTA injections were performed on average 29.3±2.7 days before surgery. Mean operative time was 252.8±101.4 minutes (range 148-395 min). Myofascial reapproximation was achieved in all cases, and there were no subsequent major preoperative or postoperative complications, including no surgical site infections. All BTA treatments were well tolerated. All patients regained normal abdominal muscle function. Mean follow-up was 18±12.8 months (range 2-36 months), and there has been no evidence of hernia recurrence in any of the patients to date.

Discussion

Elective ventral hernia operations in patients with comorbidities are costly in multiple ways. An increase in obesity and diabetes in the population has certainly made hernia repairs more challenging. Even with component separations, some defects cannot be closed and leave surgeons without good options. Bridging or inlay repair of ventral hernia defects is associated with the highest recurrence and complication rate[15,16,17]. Booth et al.[16] demonstrated that bridged repairs were associated with higher risk of hernia recurrence (56% vs 8%), as well as a higher complication rate (74% vs 32%). Any subsequent repair has a higher odds of failing and is costly both from the standpoint of quality of life and hospital charges and disability. The authors have previously demonstrated the increased cost of wound complications after complex ventral hernia repair. A complex ventral hernia repair without complications yielded $40,100 in patient charges, including inpatient charges and all inpatient and outpatient follow-up for general surgery, plastic surgery, radiology, and infectious disease. Patients with wound infections had mean charges of $85,400, and patients with mesh infections had mean charges of $146,200. This is an increased cost of over $100,000 for a mesh infection compared to a patient with no complications[25]. Although BTA charges, on average, were around $3,000, this is miniscule when compared to the cost of hernia recurrence or infection in any patient, particularly in the patients described in this case series, whose reconstruction options were extremely limited.

The application of BTA in the abdomen is one of the few promising alternatives to surgical techniques like component separation for minimizing muscle tension during abdominal wall closure after VHR[14]. Cakmak et al.[26] was the first to report on the use of BTA in the abdomen by using an animal model. The study demonstrated BTA's ability to increase abdominal wall volume and decrease muscle activity in rats, effectively alleviating abdominal pressure and decreasing the chance of abdominal compartment syndrome[26].

When other reconstructive options for VHR do not exist and a bridging mesh repair or rerelease of oblique musculature are the only options, BTA injection should be considered to decrease postoperative complications and hernia recurrence. In patients who have undergone both component separation and transverse abdominis muscle release (TAR), recurrence poses a complex challenge as lateral hernias are difficult to repair and there may be skin and subcutaneous tissue that compromises the ability to make other incisions[27].

Recent studies from Zielinski et al[28] and Ibarro-Hutardo et al[22] demonstrate the effect of BTA injected in the human abdomen. Focusing primarily on its ability to enhance primary closure, Zielinski[28] demonstrated a primary fascial closure rate of 83% in 18 patients who underwent "chemical components separation" using BTA prior to open hernia repair. Looking at actual defect size, Ibarro-Hutardo et al.[22] found an overall mean reduction of transverse hernia defect size by 5.25 ± 2.35 cm in 12 patients who received BTA injections from an original mean defect size of 13.85 ± 1.49 cm. A CT scan was performed before BTA injection and 4 weeks after, and component separation was performed in half of the cases. A follow-up study by the same group demonstrated a decrease in the thickness of the lateral abdominal wall muscles by an average of 1 cm after BTA application, and an average increase of 2.44 cm in lateral abdominal wall muscle length[14]. These changes in the abdominal wall resulting from the paralysis allowed fascial closure at the midline to be completed in all cases[14]. By decreasing midline tension through muscle paralysis, BTA has the ability to facilitate closure and diminish one of the main factors in failed hernia repairs[6].

Despite innovation in surgical techniques and meshes, large defects and previous failed repairs considerably increase the already significant chance of hernia recurrence. Considerations for future repairs, complications associated with each recurrence, quality of life of patients, and costs associated are substantial[8,9]. Recurrent repair diminishes abdominal tissue quality; the recurrence rate has been shown to increase from 24% after the first repair, to 35% and 39% after the second and third, respectively[9,12]. The present series demonstrates that preoperative BTA injection can be considered to help reduce tension in the abdominal wall musculature and allow for fascial closure, an important predictor of success in hernia repair. While BTA's predominant use over the last 40 years has been in spastic muscle disorders and cosmetic procedures, recent additional studies[29], as well as the present study, demonstrate BTA as an adjunct for abdominal wall surgery.

In addition, BTA has also been shown to have potential as a successful pain modulator. Smoot et al.[30] reported a case study in which patient's postoperative pain improved substantially after BTA injection. Zendejas et al[31] performed a quantitative experiment, examining opioid usage and postoperative pain. When comparing 24 patients who underwent BTA injections to patients who had not, they reported a 64% reduction in opioid usage on fifth postoperative day in patients who underwent the BTA treatment.

These four cases illustrate unique examples where complex abdominal wall reconstruction can be greatly aided with BTA and is likely in part responsible for good patient outcomes. BTA should be studied further in appropriate patients and with long term follow-up.

Conclusion

Preoperative BTA injection is a safe and an effective method to obtain myofascial reapproximation and should be considered for complex abdominal wall reconstruction to avoid fascial bridging, especially in cases where previous component separation had been performed and with very large hernias with loss of domain. Defining the appropriate population is the goal of this study. BTA in patients undergoing abdominal surgery holds a promise and merits further investigation in hernia repair.

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